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# Synthesis of New Secoprostaglandins as Inducers of Platelet Aggregation[1]

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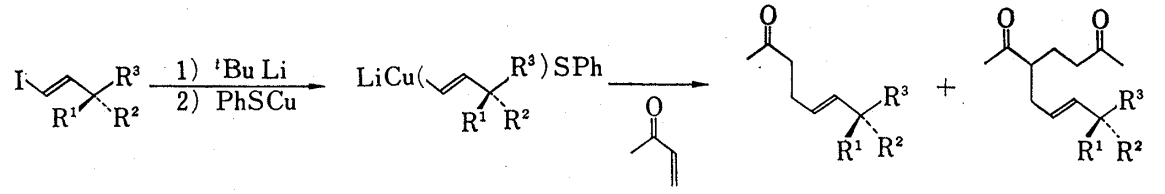
Two series of 8-acetyl-12-hydroxyalkadienoic acids and 14-hydroxy-9-oxoalkadienoic acids, which can be regarded as 11,12- and 8,12-secoprostaglandin $E_2$, were synthesized and evaluated for biological activity on platelet function. Key members of each series, 11,12- and 8,12-seco-11-norprostaglandin $E_2$, were found to induce platelet aggregation. This effect was inhibited by preincubation of PRP with prostaglandin $I_2$ but was not inhibited by indomethacin.

**Keywords**——secoprostaglandin; oxygenated polyunsaturated fatty acid; Michael addition; alkylation; inducer of platelet aggregation; $TXA_2$-like activity

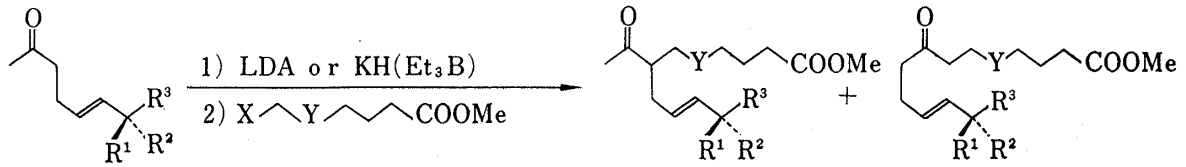
Arachidonic acid (AA) is known to be metabolized through the well-known AA cascade in almost every animal cell or tissue to form biologically important substances, *e.g.*, primary prostaglandins (PGs), PG-endoperoxides, thromboxane $A_2$ ($TXA_2$), prostacyclin ($PGI_2$), hydroxylated unsaturated fatty acids, and leukotrienes.[2,3] The discovery of $TXA_2$[4] and $PGI_2$[5] led to an understanding of new aspects of the interaction of platelets with the arterial wall.[6] Increasing interest is being directed toward natural hydro(per)oxylated unsaturated fatty acids, because the biosynthesis of $TXA_2$ and $PGI_2$ is presumably regulated under negative feedback control by 12- and 15-hydro(per)oxy-5,8,10,14-eicosatetraenoic acid (12-H(P)ETE[7] and 15-H(P)ETE[8]), respectively. It is known that 12-hydroxy-5,8,10-heptadecatrienoic acid (HHT) formed from PG- endoperoxide has a leukocyte chemotactic activity.[9] Recently, the structure of leukotrienes was elucidated; they are noteworthy new metabolites of AA and show unique biological activities.[10] The series of leukotrienes can be regarded as oxygenated unsaturated fatty acids. Thus, modification of unsaturated fatty acid derivatives might be a promising approach to the design of new biologically active compounds. This concept prompted us to synthesize polyunsaturated fatty acids prossessing serveal functional groups characteristic of primary PGs. Previously, Merck researchers.have reported the preparation of several kinds of secoprostaglandins including 11,12-seco $PGE_1$ derivatives which stimulate cAMP formation in the mouse ovary assay.[11] We synthesized two series of new 8-acetyl-12-hydroxyalkadienoic acids and 14-hydroxy-9-oxoalkadienoic acids, *i.e.*, 11,12- and 8,12-seco $PGE_2$ derivatives, and their biological properties were investigated.

Twelve acylhydroxyalkadienoic acid derivatives and five hydroxyoxoalkadienoic acid derivatives were synthesized. 8-Acetyl-12-hydroxyalkadienoic acids (**9**) and 14-hydroxy-9-oxoalkadienoic acids (**10**) were synthesized as shown in Chart 1, followed by deprotection. Chiral vinyl iodides (**1a, b**) were prepared by resolving the racemates according to modification of the reported procedures.[12] The resulting vinyl iodides (**1a—d**) were converted into mixed vinyl cuprates (**2a—d**) by treatment with *t*-butyllithium and then phenylthiocopper.[13] The mixed vinyl cuprates (**2a—d**) were allowed to react *in situ* with methyl vinyl ketone to furnish conjugate addition products (**3**) accompanied by small amounts of further conjugate adducts (**3'**).[14] Alkylation of ketones (**3**) with halides (**4**) was carried out using two different bases, *i.e.*, lithium diisopropylamide (method A) and potassium hydride-triethylborane[15] (method B). Each alkylation resulted in the formation of the thermodynamically controlled product (**5**) and the kinetically controlled product (**6**) in variable ratios depending upon the reaction conditions.[16] Acidic hydrolysis of silyloxy esters (**5a—c** and **6a—c**) yielded corresponding




**1a—d** **2a—d** **3a—d** **3′**

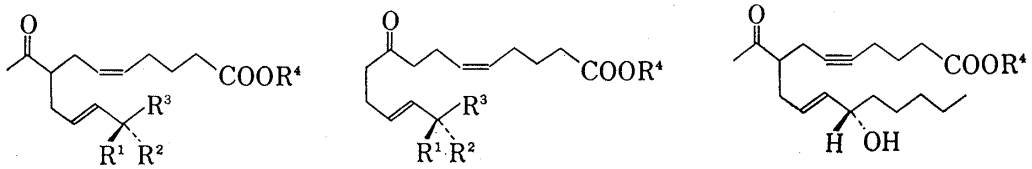
**a**(*S*): $R^1$=H; $R^2$=$OSiMe_2$ $^t$Bu; $R^3$=$C_5H_{11}$
**a**(*R*): $R^1$=$OSiMe_2$ $^t$Bu; $R^2$=H; $R^3$=$C_5H_{11}$
**b**(*S*): $R^1$=H; $R^2$=$OSiMe_2$ $^t$Bu; $R^3$=cyclohexyl
**b**(*R*): $R^1$=$OSiMe_2$ $^t$Bu; $R^2$=H; $R^3$=cyclohexyl
*dl*-**c**: $R^1$, $R^2$=(Me, $OSiMe_2$ $^t$Bu); $R^3$=$C_5H_{11}$
**d**: $R^1$=$R^2$=H; $R^3$=$C_5H_{11}$




**3a—d** **4g—i** **5a—d** **6a—d**

**4g**: X=I; Y=*cis* CH=CH
**4h**: X=Br; Y=*cis* CH=CH
**4i**: X=Br; Y=C≡C

Chart 1




**7a—c**: $R^4$=Me
**9a—d**: $R^4$=H

**8a—c**: $R^4$=Me
**10a—d**: $R^4$=H

**7a′**(*S*): $R^4$=Me
**9a′**(*S*): $R^4$=H

**a**(*S*): $R^1$=H; $R^2$=OH; $R^3$=$C_5H_{11}$
**a**(*R*): $R^1$=OH; $R^2$=H; $R^3$=$C_5H_{11}$
**b**(*S*): $R^1$=H; $R^2$=OH; $R^3$=cyclohexyl
**b**(*R*): $R^1$=OH; $R^2$=H; $R^3$=cyclohexyl
*dl*-**c**: $R^1$, $R^2$=(Me, OH); $R^3$=$C_5H_{11}$
**d**: $R^1$, $R^2$=H; $R^3$=$C_5H_{11}$

Chart 2

hydroxy esters (**7a—c** and **8a—c**).[17] Saponification of the hydroxy esters (**7** and **8**) gave acids (**9** and **10**, respectively). Acetylenic derivatives (**7a′**(*S*), **9a′**(*S*)) were prepared by similar alkylation of ketone (**3a** (*S*)) with bromide (**4i**) followed by saponification as described above.

In Chart 3, similar conjugate additions of the mixed cuprate (**2a** (*S*)) to crotyl methyl ketone (**11e**) and ethyl vinyl ketone (**11f**) were carried out to afford the corresponding adducts (**12e, f**). The adducts were alkylated by method A or B to form silyloxy esters (**13e, f**) accompanied by small amounts of the positional isomers (**14**). The synthesis of hydroxy acids (**16e, f**), *i.e.*, 10,11-seco-11-deoxy $PGE_2$, was achieved by acidic hydrolysis of **13e, f** and successive saponification of the desilylated products (**15e, f**).

An alternative method to prepare the alkylated products (**5**) involves the one-pot direct alkylation of $\beta$-alkenylated enolates generated by conjugate addition of mixed cuprates to $\alpha,\beta$-unsaturated ketones. Direct alkylation of such copper enolates with halides (**4**) for

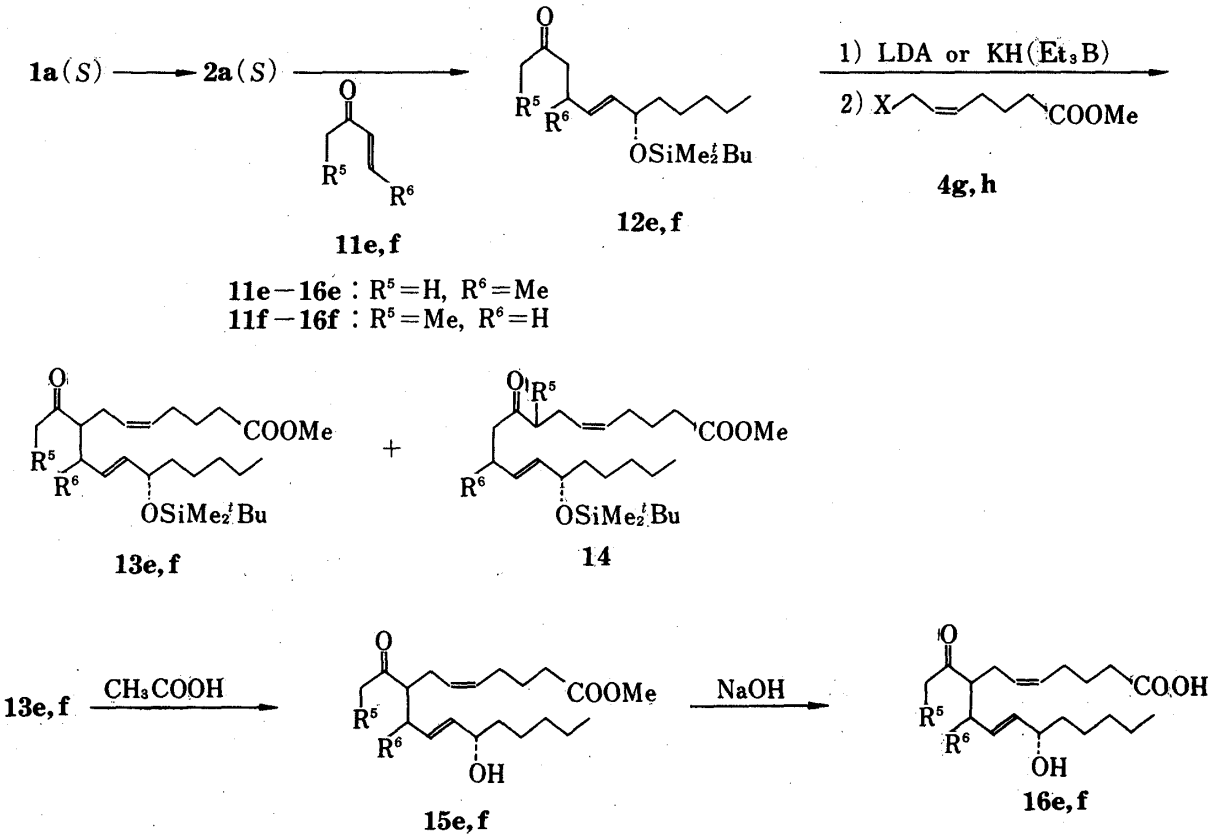



Chart 3

prostaglandin synthesis has been investigated without success to construct PG skeleton,[18] although such an enolate derived from protected 4-hydroxy-2-cyclopentenone has been reported to be acylated with acyl chlorides to produce 7-keto $PGE_1$ derivatives.[19] Conjugate addition of the mixed cuprate (*dl*-**2a**) to methyl vinyl ketone resulted in the formation of the enolate intermediate (**17**), which was allowed to react *in situ* with methyl (5*Z*)-7-iodo-5-heptenoate (**4g**) to give the regiospecifically vicinally dialkylated product (*dl*-**5a**) (Chart 4).[18a]

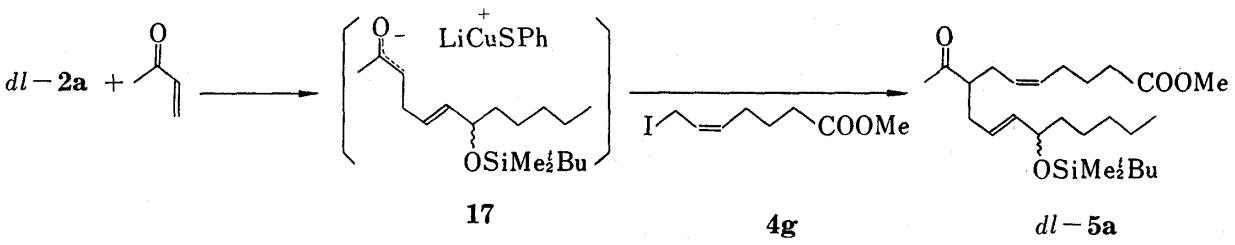
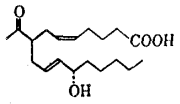
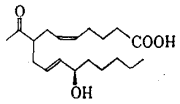
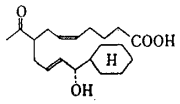
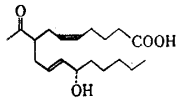
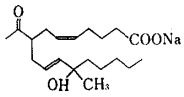
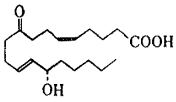



Chart 4

In order to study the effect of the carbonyl function in the products on biological activities, a typical compound (**5a**(*S*)) was modified by reduction or methoxime formation at the acetyl carbonyl function. Reduction of **5a**(*S*) with sodium borohydride followed by desilylation with acetic acid or *vice versa* gave the dihydroxy acid (**20**). The methoxime derivative (**26**) was prepared by derivatization of the desilylated ketone of **5a**(*S*) with methoxylamine hydrochloride and subsequent ester-hydrolysis of the methoxime ester.

Another modification of **9a**(*S*) was carried out by conversion of the 5*Z* double bond to provide the 6-keto-derivative because the corresponding parent compound, 6-keto $PGE_1$, has

Table I. Activities to Induce Platelet Aggregation

| Compd | Structure | Platelet aggregation (%) 10 μg/ml | 30 μg/ml | 100 μg/ml |
|---|---|---|---|---|
| **9a**(*S*) |  | 0 | 22.3±4.0 | 56.1±1.1 |
| **9a**(*R*) |  | | 0 | 28.5±1.8 |
| **9b**(*S*) |  | | 0 | 16.4±1.6 |
| **9a′**(*S*) |  | | 0 | 7.1±0.4 |
| *dl*-**9c**-Na |  | 38.1±2.2 | 58.3±2.2 | 64.1±1.5 |
| **10a**(*S*) |  | 0 | 11.3±1.5 | 51.3±1.2 |

interesting biological activities.[20] The synthesis of the 6-keto acid (**24**) was performed by the following sequence:[21] (1) sodium borohydride reduction of **5a**(*S*); (2) iodoetheration of **18**; (3) treatment of **21** with DBN and successive exposure of the resulting vinyl ether to aqueous acetic acid; (4) oxidation of **22** with $CrO_3$ in pyridine; (5) desilylation of **23** with aqueous acetic acid, as shown in Chart 5.

When chiral ketones (**3a**—**c** and **12e**, **f**) are alkylated with halides (**4**) on each prochiral carbon atom at the α-position with respect to the carbonyl group, the products (**5a**—**c** and **13e**, **f**) should consist of two or more stereoisomers in equal quantities. This is similar to conjugate addition of chiral cuprate to crotyl methyl ketone. Because these two or more isomers could not be clearly separated on TLC despite the appearance of clear diastereomeric signals in the nuclear magnetic resonance (NMR) spectra, biological activities were assayed as diastereomeric mixtures without further separation. The structures of all products are supported by their infrared (IR), NMR, mass, and high-resolution mass spectra and in each case the purity was checked by TLC. The final products were confirmed to be homogeneous by TLC.

According to preliminary biological evaluation,[22] the novel unsaturated fatty acid derivatives induced platelet aggregation dose-dependently, as shown in Table I. The aggregating activity of **9a**(*S*) was nearly equipotent to that of arachidonic acid (AA). The aggregation induced by **9a**(*S*) was inhibited by $PGI_2$, but not by indomethacin, while AA-induced aggregation was inhibited by $PGI_2$ and indomethacin. Interestingly, **9a**(*S*) was found to have $TXA_2$-like activity by Langendorff's technique using isolated tissues. Thus, novel synthetic fatty acids such as **9a**(*S*) could be useful as pharmacological tools in the investigation of the biological role of $TXA_2$ in myocardial ischemia.

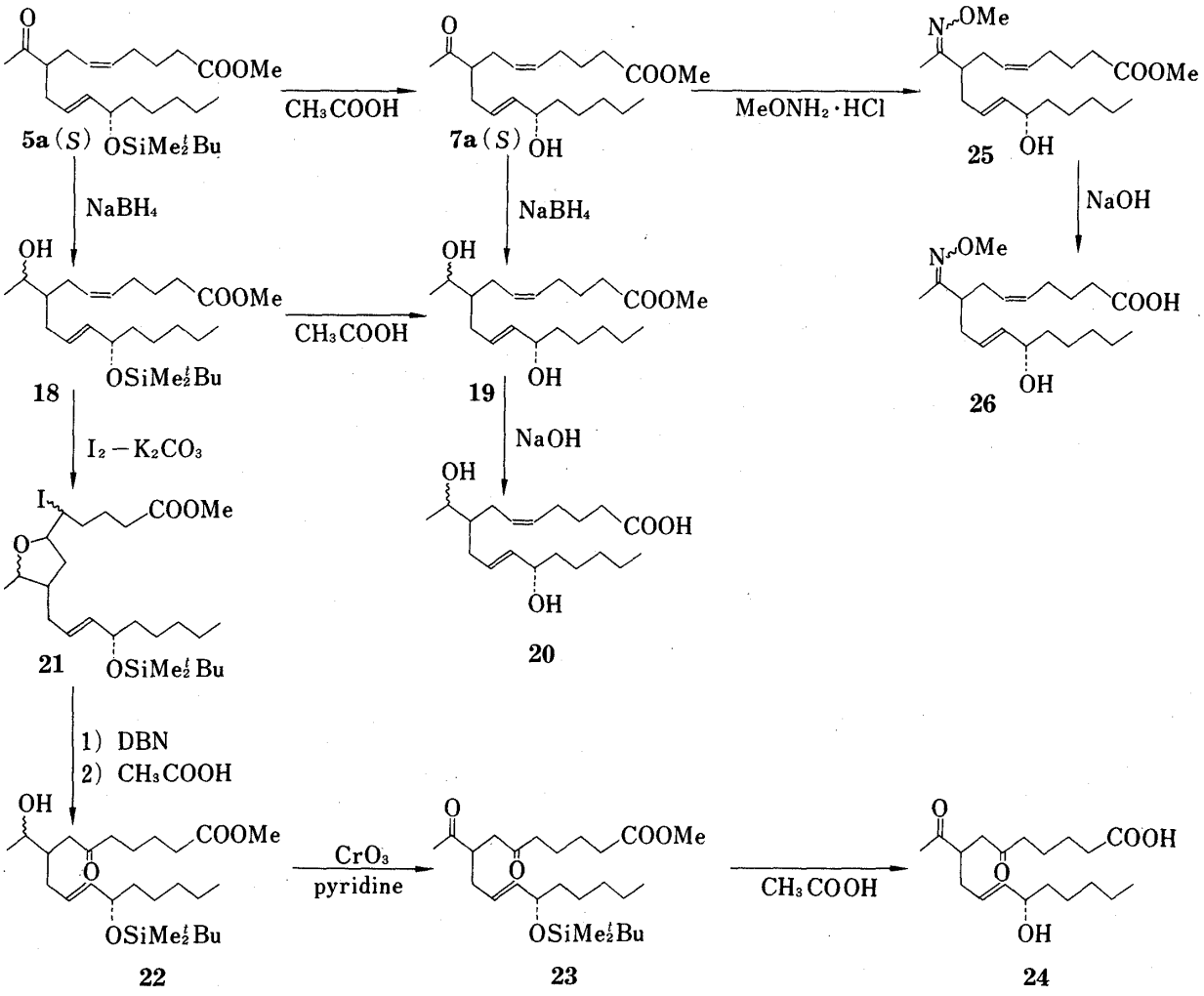



Chart 5

## Experimental

IR spectra were recorded on a JASCO A102 spectrometer. $^1$H-NMR spectra were taken on a Varian EM 360A (60 MHz) spectrometer in $CCl_4$ or $CDCl_3$. Chemical shifts are reported as parts per million relative to $Me_4Si$ as an internal standard. The following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet, b, broad. Mass spectra were obtained on a Shimadzu LKB 9000 spectrometer (70 eV unless otherwise noted). When molecular ions were too weak to be detected, other characteristic peaks were indicated. High-resolution mass spectra were measured on a JEOL JMS D 300 mass spectrometer for dehydration peaks. Optical rotations were measured on a JASCO DIP-SL automatic polarimeter.

Layer chromatography was performed on Merck silica gel (Kieselgel 60 $F_{254}$) analytical (thickness 0.25 mm) and preparative (0.5 mm and 2.0 mm) plates. Column chromatography was carried out on Wako gel C-200 silica gel or silica Woelm TSC (silica gel for dry-column chromatography). Unless otherwise specified, all reactions were carried out under an atmosphere of argon or nitrogen.

Chromatographed compounds were prepared for analysis and biological testing by being heated at 40°C *in vacuo* for 1—2 h in order to remove the last traces of solvents. However, all the intermediates and final products are viscous oils that retain solvents tenaciously. It was impossible to remove the solvents completely from these compounds, since they decomposed partially under normal drying conditions suitable for elemental analysis.

**(5*Z*,10*E*)-(8*RS*,12*S*)-8-Acetyl-12-hydroxy-5,10-heptadecadienoic Acid (9a(*S*)) and (5*Z*,12*E*)-(14*S*)-9-Oxo-14-hydroxy-5,12-nonadecadienoic Acid (10a(*S*))**——(a) (5*Z*)-(7*S*)-7-*tert*-Butyldimethylsilyloxy-5-dodecan-2-one (3a(*S*)): A 1.9 M pentane solution of *tert*-BuLi[17,19] (8.9 ml, 17 mmol) was added at −78°C to a stirred solution of (1*Z*)-(3*S*)-*tert*-butyldimethylsilyloxy-1-iodo-1-octene (1a(*S*); 3.10 g, 8.42 mmol, $[\alpha]_D^{20}$ −28.9° ($c$=3.91, $CCl_4$)) prepared by silylation of (1*Z*)-(3*S*)-3-hydroxy-1-iodo-1-octene[12] ($[\alpha]_D^{20}$ +10.4° ($c$=3.88, (MeOH)) in ether 30 ml), and the resulting mixture was stirred at −78°C for 2 h. A solution of phenylthiocopper[13] (1.38 g, 8.0 mmol) and $(Me_2N)_3P$ (2.70 g, 16.0 mmol) in ether (5 ml) was then added at −78°C.

The whole was stirred at −78°C for 1 h, then methyl vinyl ketone (560 mg, 8.0 mmol) in ether (2 ml) was added at −78°C, and the mixture was stirred at −78°C for 10 min, then at −40°C for 1 h. The reaction was quenched by the addition of saturated aqueous $NH_4Cl$ at −40°C. The mixture was diluted with ether (100 ml), then washed with aqueous ammoniacal $NH_4Cl$ and saturated aqueous $NH_4Cl$. The separated organic layer was dried over $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed on silica gel (100 g) with cyclohexane–ethyl acetate (9: 1) to give **3a**(*S*) (975 mg, 3.13 mmol, 39.1%) and (7*Z*)-(5*RS*,9*S*)-5-acetyl-9-*tert*-butyldimethylsilyloxytetradec-7-en-2-one (**3a′**(*S*); 317 mg, 0.83 mmol, 10.4%) as the double Michael addition product. **3a**(*S*); IR $\nu_{max}^{neat}$ $cm^{-1}$: 1720, 1460, 1360, 1260, 1080, 975, 840, 780. NMR ($CCl_4$) $\delta$: 0.08 (6H, s, $SiMe_2$), 0.84 (12H, s+m, $^t$Bu and $C_{14}H_3$), 1.3 (8H, m), 2.03 (3H, s, $COCH_3$), 2.2—2.5 (4H, m, $C_3H_2$ and $C_4H_2$), 3.97 (1H, m, $C_7H$), 5.4 (2H, m, olefinic H). **3a′**(*S*); NMR ($CDCl_3$) $\delta$: 0.03 (6H, s, $SiMe_2$), 0.88 (12H, s+m, $^t$Bu and $C_{14}H_3$), 1.1—1.4 (10H, m), 2.09 (6H, s, $COCH_3$), 2.1—2.6 (5H, m), 4.00 (1H, m, $C_9H$), 5.35—5.55 (2H, m, olefinic H). $[\alpha]_D^{20}$ −7.0° (*c*=9.35, MeOH).

(b) Methyl (5*Z*,10*E*)-(8*RS*,12*S*)-8-Acetyl-12-*tert*-butyldimethylsilyloxy-5,10-heptadecadienoate (**5a**(*S*)) and Methyl (5*Z*,12*E*)-(14*S*)-*tert*-Butyldimethylsilyloxy-9-oxo-5,12-nonadecadienoate (**6a**(*S*)): Method A: *n*-BuLi (1.4 M, 0.86 ml, 1.20 mmol) in hexane was added to a stirred solution of diisopropylamine (121 mg, 1.20 mmol) in THF (3 ml) at −78°C, and the mixture was stirred at −78°C for 10 min. Next, a solution of the ketone (**3a**(*S*); 312 mg, 1.0 mmol) in THF (2 ml) was added at −78°C, and the whole was stirred at −78°C for 10 min, then at −20°C for 10 min. Methyl (5*Z*)-7-iodo-5-heptenoate (**4g**; 348 mg, 1.30 mmol) was added to the mixture at −20°C, and the resulting solution was stirred at −20°C for 20 min, and then at room temperature for 1 h. The reaction was quenched by the addition of saturated aqueous $NH_4Cl$. The organic layer was taken up in ether (100 ml), washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to leave 630 mg of an oily residue. Separation by preparative TLC (cyclohexane: ethyl acetate=85: 15) gave **5a**(*S*) (110 mg, 0.243 mmol, 24.3%) and **6a**(*S*) (67 mg, 0.148 mmol), 14.8%). **5a**(*S*): *Rf* 0.35 (hexane: ether=4: 1). IR $\nu_{max}^{neat}$ $cm^{-1}$: 1735, 1710, 1460, 1435, 1360, 1245, 1160, 1080, 965, 835, 775. NMR ($CDCl_3$) $\delta$: 0.08 (6H, s, $SiMe_2$), 0.90 (12H, s+m, $^t$Bu and $C_{17}H_3$), 1.1—1.7 (10H, m), 1.8—2.4 (9H, m), 2.08 (3H, s, $COCH_3$), 3.63 (3H, s, $COOCH_3$), 3.7—4.1 (1H, m, $C_{12}H$), 5.35 (4H, m, olefinic H). MS (20 eV) *m/e*: 437 (M−Me), 409 (M−$COCH_3$), 395 (M−$^t$Bu). **6a**(*S*); *Rf* 0.40 (hexane: ether=4: 1). IR $\nu_{max}^{neat}$ $cm^{-1}$: 1740, 1720, 1440, 1360, 1250, 1205, 1170, 1080, 970, 840, 780. NMR ($CDCl_3$) $\delta$: 0.02 (6H, s, $SiMe_2$), 0.82 (12H, s+m, $^t$Bu and $C_{19}H_3$), 1.23 (10H, m), 1.8—2.4 (12H, m), 3.63 (3H, s, $COOCH_3$), 3.65—4.15 (1H, m, $C_{14}H$), 5.35 (4H, m, olefinic H). MS (20 eV) *m/e*: 437 (M−Me), 395 (M−$^t$Bu).

(c) Methyl (5*Z*,10*E*)-(8*RS*,12*S*)-8-Acetyl-12-hydroxy-5,10-heptadecadienoate (**7a**(*S*)) and Methyl (5*Z*,12*E*)-(14*S*)-9-Oxo-14-hydroxy-5,12-nonadecadienoate (**8a**(*S*)): The silyloxy ester (**5a**(*S*); 110 mg, 0.24 mmol) was dissolved in a mixture of AcOH (3 ml), water (1 ml), and THF (1 ml). After being stirred at room temperature for 18 h, the mixture was diluted with AcOEt (50 ml), neutralized with saturated aqueous $NaHCO_3$, washed with brine, and dried ($MgSO_4$). Evaporation of the solvent left the hydroxy ester (**7a**(*S*); 78 mg, 0.23 mmol, 96%) as a colorless oil showing one spot on TLC (*Rf* 0.40, cyclohexane: ethyl acetate=3: 2). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3300, 1735, 1715, 970. NMR ($CCl_4$) $\delta$: 0.90 (3H, t, *J*=7 Hz, $C_{17}H_3$), 1.3 (10H, m), 1.8—2.5 (9H, m), 2.00 (3H, s, $COCH_3$), 3.60 (3H, s, $COOCH_3$), 3.65 (1H, bs, OH), 3.90 (1H, bs, $C_{12}H$), 5.35 (4H, m, olefinic H). MS *m/e*: 320 (M−$H_2O$). $[\alpha]_D^{20}$ +2.8° (*c*=6.13, MeOH). High-resolution MS for $C_{20}H_{32}O_3$ (dehydration peak from molecular ion): Calcd *m/e*: 320.2354; Found: 320.2355.

Similar acidic hydrolysis of the other silyloxy ester **6a**(*S*) (67 mg, 0.148 mmol) gave the hydroxy ester **8a**(*S*) (48 mg, 0.142 mmol, 96%): *Rf* 0.45 (cyclohexane: ethyl acetate=3: 2). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3400, 1740, 1720, 970. NMR ($CCl_4$) $\delta$: 0.86 (3H, m, $C_{19}H_3$), 1.3 (10H, m), 1.8—2.5 (12H, m), 3.60 (3H, s, $COOCH_3$), 3.8—4.1 (1H, m, $C_{14}H$), 5.2—5.6 (4H, m, olefinic H). MS *m/e*: 320 (M−$H_2O$), 289. $[\alpha]_D^{20}$ +2.9° (*c*=3.47, MeOH). High-resolution MS for $C_{20}H_{32}O_3$ (dehydration peak from molecular ion): Calcd *m/e*: 320.2354; Found: 320.2359.

(d) (5*E*,10*Z*)-(8*RS*,12*S*)-8-Acetyl-12-hydroxy-5,10-heptadecadienoic Acid (**9a**(*S*)) and (5*E*,12*Z*)-(14*S*)-9-Oxo-14-hydroxy-5,12-nonadecadienoic Acid (**10a**(*S*)): A solution of **7a**(*S*) (70 mg, 0.21 mmol) in MeOH (1 ml) and 1 N NaOH solution (0.3 ml, 0.30 mmol) was allowed to stand at room temperature for 12 h. Most of the MeOH was evaporated off and the residual solution was acidified with 1 N hydrochloric acid. The acidic product was taken up in AcOEt and dried over $MgSO_4$. Removal of the solvent yielded almost pure acid (**9a**(*S*); 55 mg, 0.17 mmol, 81.0%). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3300, 1720. NMR ($CDCl_3$) $\delta$: 0.90 (3H, t, *J*=7 Hz, $C_{17}H_3$), 1.3 (10H, m), 1.8—2.5 (9H, m), 2.05 (3H, s, $COCH_3$), 4.00 (1H, m, $C_{12}H$), 5.4 (4H, m, olefinic H), 6.2 (2H, bs, OH and COOH).

Similar saponification of the other ester (**8a**(*S*); 48 mg, 0.142 mmol) gave **10a**(*S*) (43 mg, 0.133 mmol, 93.7%). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3200, 1710. NMR ($CDCl_3$) $\delta$: 0.86 (3H, m, $C_{19}H_3$), 1.3 (10H, m), 1.8—2.5 (12H, m), 3.8—4.2 (1H, m, $C_{14}H$), 5.2—5.6 (4H, m, olefinic H), 6.70 (2H, bs, OH and COOH).

**(5*Z*,10*E*)-(8*RS*,12*R*)-8-Acetyl-12-hydroxy-5,10-heptadecadienoic Acid (9a(*R*)) and (5*Z*,12*E*)-(14*R*)-9-Oxo-14-hydroxy-5,12-nonadecadienoic Acid (10a(*S*))**——(a) (5*Z*)-(7*R*)-7-*tert*-Butyldimethylsilyloxy-5-dodecen-2-one (**3a**(*R*)): (1*Z*)-(3*R*)-3-*tert*-butyldimethylsilyloxy-1-iodo-1-octene (**1a**(*R*); $[\alpha]_D^{23}$ +29.3° (*c*=3.75, $CCl_4$) was prepared by silylation of (1*Z*)-(3*R*)-3-hydroxy-1-iodo-1-octene ($[\alpha]_D^{23}$ −9.4° (*c*=5.19, MeOH)), which was obtained by a similar resolution method[12] using (+)-α-methylbenzylamine. Similar β-addition of the mixed cuprate (**2a**(*R*)) prepared from **1a**(*R*) to methyl vinyl ketone gave the ketone (**3a**(*R*)) in 41.3% yield.

IR $\nu_{max}^{neat}$ $cm^{-1}$: 1720, 1460, 1360, 1260, 1080, 975, 840, 780. NMR ($CCl_4$) $\delta$: 0.08 (6H, s, $SiMe_2$), 0.84 (12H, s+m, $^t$Bu and $C_{12}H_3$), 1.27 (8H, m), 2.06 (3H, s, $COCH_3$), 2.2—2.5 (4H, m, $C_3H_2$ and $C_4H_2$), 3.95 (1H, m, $C_7H$), 5.3—5.5 (2H, m, olefinic H).

(b) Methyl (5*Z*,10*E*)-(8*RS*,12*R*)-8-Acetyl-12-*tert*-butyldimethylsilyloxy-5,10-heptadecadienoate (**5a**(*R*)) and Methyl (5*Z*,12*E*)-(14*S*)-9-Oxo-14(S)-*tert*-butyldimethylsilyloxy-5,12-nonadecadienoate (**6a**(*R*)): Method B: A solution of **3a**(*R*) (644 mg, 2.06 mmol) in THF (3 ml) was added at 0°C to a suspension of KH (23% in mineral oil, 522 mg, 3.0 mmol) which had been washed with dry pentane (30 ml), and the mixture was stirred at room temperature for 20 min, then a 1 M THF solution of $Et_3B$ (4.0 ml, 4.0 mmol) was added.[15] Stirring was continued at room temperature for 10 min. A solution of methyl (5*Z*)-7-bromo-5-heptenoate (**4h**; 546 mg, 2.47 mmol) in THF (2 ml) was then added and the mixture was stirred at ambient temperature for 2 h. Brine (50 ml) was added and the whole was extracted with AcOEt (2 × 100 ml). The combined extracts were washed with brine (50 ml), dried over $MgSO_4$, and concentrated *in vacuo* to afford 1.02 g of a crude product. Preparative TLC separation (hexane: ether=3: 1) provided **5a**(*R*) (219 mg, 0.485 mmol, 23.5%) and **6a**(*R*) (163 mg, 0.361 mmol, 17.5%). **5a**(*R*); *Rf* 0.35 (hexane: ether=4: 1). IR $\nu_{max}^{neat}$ $cm^{-1}$: 1740, 1710, 1460, 1435, 1360, 1245, 1160, 1080, 965, 835, 775. NMR ($CCl_4$) $\delta$: 0.02 (6H, s, $SiMe_2$), 0.84 (12H, s+m, $^t$Bu and $C_{17}H_3$), 1.1—1.7 (10H, m), 1.8—2.4 (9H, m), 1.97 (3H, s, $COCH_3$), 3.55 (3H, s, $COOCH_3$), 3.93 (1H, m, $C_{12}H$), 5.15—5.40 (4H, m, olefinic H). MS (20 eV) *m/e*: 437 (M−Me), 409 (M−$COCH_3$), 395 (M−$^t$Bu). **6a**(*R*); *Rf* 0.40 (hexane: ether=4: 1). IR $\nu_{max}^{neat}$ $cm^{-1}$: 1740, 1720, 1440, 1360, 1250, 1205, 1170, 1080, 970, 840, 780. NMR ($CCl_4$) $\delta$: 0.02 (6H, s, $SiMe_2$), 0.82 (12H, s+m, $^t$Bu and $C_{19}H_3$), 1.23 (10H, m), 1.8—2.35 (12H, m), 3.53 (3H, s, $COOCH_3$), 3.90 (1H, m, $C_{14}H$), 5.2—5.4 (4H, m, olefinic H). MS (20 eV) *m/e*: 437 (M−Me), 395 (M−$^t$Bu).

(c) Methyl (5*Z*,10*E*)-(8*RS*,12*R*)-8-Acetyl-12-hydroxy-5,10-heptadecadienoate (**7a**(*R*)) and Methyl (5*Z*,12*E*)-(14*R*)-9-Oxo-14-hydroxy-5,12-nonadecadienoate (**8a**(*R*)): Similar acidic hydrolysis of **5a**(*R*) (219 mg, 0.485 mmol) and **6a**(*R*) (163 mg, 0.361 mmol) gave **7a**(*R*) (161 mg, 0.476 mmol, 98.2%) and **8a**(*R*) (66 mg, 0.195 mmol, 54.0%), respectively. **7a**(*R*); IR $\nu_{max}^{neat}$ $cm^{-1}$: 3470, 1735, 1710, 1440, 1360, 1165, 970. NMR ($CDCl_3$) $\delta$: 0.86 (3H, m, $C_{17}H_3$), 1.3 (10H, m), 1.8—2.5 (9H, m), 2.06 (3H, s, $COCH_3$), 3.61 (3H, s, $COOCH_3$), 3.95 (1H, m, $C_{12}H$), 5.2—5.6 (4H, m, olefinic H). MS *m/e*: 320 (M−$H_2O$). High-resolution MS for $C_{20}H_{32}O_3$ (dehydration peak from molecular ion): Calcd *m/e*: 320.2354; Found: 320.2361. **8a**(*R*); IR $\nu_{max}^{neat}$ $cm^{-1}$: 3460, 1735, 1710, 1435, 1360, 1245, 1215, 1160, 970. NMR ($CDCl_3$) $\delta$: 0.86 (3H, m, $C_{19}H_3$), 1.3 (10H, m), 1.8—2.5 (12H, m), 3.61 (3H, s, $COOCH_3$), 3.95 (1H, m, $C_{14}H$), 5.2—5.6 (4H, m, olefinic H). MS *m/e*: 320 (M−$H_2O$), 289. High-resolution MS for $C_{20}H_{32}O_3$ (dehydration peak from molecular ion): Calcd *m/e*: 320.2354; Found: 320.2358.

(d) (5*Z*,10*E*)-(8*RS*,12*R*)-8-Acetyl-12-hydroxy-5,10-heptadecadienoic Acid (**9a**(*R*)) and (5*Z*,12*E*)-(14*R*)-9-Oxo-14-hydroxy-5,12-nonadecadienoic Acid (**10a**(*R*)): **7a**(*R*) (60 mg, 0.178 mmol) and **8a**(*R*) (66 mg, 0.195 mmol) were similarly hydrolyzed with NaOH to yield **9a**(*R*) (57 mg, 0.176 mmol, 98.8%) and **10a**(*R*) (62 mg, 0.191 mmol, 98.1%), respectively. **9a**(*R*); IR $\nu_{max}^{neat}$ $cm^{-1}$: 3300, 1720. NMR ($CDCl_3$) $\delta$: 0.86 (3H, m, $C_{17}H_3$), 1.3 (10H, m), 1.8—2.5 (9H, m), 2.05 and 2.07 (total 3H, 2s, diastereomeric $COCH_3$), 4.00 (1H, m, $C_{12}H$), 5.15—5.55 (4H, m, olefinic H), 6.10 (2H, bs, OH and COOH). **10a**(*R*); IR $\nu_{max}^{neat}$ $cm^{-1}$: 3200, 1710. NMR ($CDCl_3$) $\delta$: 0.86 (3H, m, $C_{19}H_3$), 1.3 (10H, m), 1.8—2.5 (12H, m), 4.00 (1H, m, $C_{14}H$), 5.2—5.6 (4H, m, olefinic H), 6.03 (2H, bs, OH and COOH).

**Methyl (5*Z*,10*E*)-(8*RS*,12*RS*)-8-Acetyl-12-tert-butyldimethylsilyloxy-5,10-heptadecadienoate (*dl*-5a)**——An alternative preparation of *dl*-**5a** was carried out as follows. In a manner similar to that described for **3a**(*S*), conjugate addition of mixed cuprate (*dl*-**2a**) prepared from *dl*-**1a** (850 mg, 2.3 mmol) to methyl vinyl ketone (147 mg, 2.1 mmol) occurred regiospecifically to give the enolate anion (**17**) *in situ*. Next, a solution of **4g** (670 mg, 2.5 mmol) in THF (3 ml) and HMPA (2 ml) was added at −40°C, and the mixture was stirred at −20°C for 2.5 h. The usual work-up and purification by preparative TLC yielded *dl*-**5a** (60 mg, 0.12 mmol, 6%), which was identical (TLC, IR, NMR, and MS) with **5a**(*S*) and **5a**(*R*) as described above.

**(5*Z*,10*E*)-(8*RS*,12*S*)-8-Acetyl-12-cyclohexyl-12-hydroxy-5,10-dodecadienoic Acid (9b(*S*))**——(a) (5*E*)-(7*S*)-7-*tert*-Butyldimethylsilyloxy-7-cyclohexyl-5-hepten-2-one (**3b**(*S*)): (1*E*)-(3*S*)-3-*tert*-butyldimethylsilyloxy-3-cyclohexyl-1-iodo-1-propene (**1b**(*S*); $[\alpha]_D^{18}$ −19.5° (*c*=3.71, $CCl_4$)) was analogously prepared by silylation of (+)-(1*E*)-(3*S*)-3-cyclohexyl-3-hydroxy-1-iodo-1-propene, which was obtained by similar preparation and resolution procedure[12] using (−)-α-methylbenzylamine. In a similar manner, conjugate addition of **2b**(*S*) to methyl vinyl ketone gave **3b**(*S*) in 29.4% yield. IR $\nu_{max}^{neat}$ $cm^{-1}$: 1720, 1670, 1450, 1360, 1250, 1090, 1050, 835, 775. NMR ($CDCl_3$) $\delta$: 0.08 (6H, s, $SiMe_2$), 0.85 (9H, s, $^t$Bu), 0.9—1.9 (11H, m), 2.08 (3H, s, $COCH_3$), 2.15—2.50 (4H, m, $C_3H_2$ and $C_4H_2$), 3.67 (1H, m, $C_7H$), 5.3—5.5 (2H, m, olefinic H).

(b) Methyl (5*Z*,10*E*)-(8*RS*,12*S*)-8-Acetyl-12-*tert*-butyldimethylsilyloxy-12-cyclohexyl-5,10-dodecadienoate (**5b**(*S*)) and Methyl (5*Z*,12*E*)-(14*S*)-14-*tert*-Butyldimethylsilyloxy-14-cyclohexyl-9-oxo-5,12-tetradecadienoate (**6b**(*S*)): Reaction of **3b**(*S*) (157 mg, 0.48 mmol) and **4g** (162 mg, 0.6 mmol) by method A gave **5b**(*S*) (41 mg, 0.088 mmol, 18.4%) and **6b**(*S*) (93 mg, 0.20 mmol, 41.8%). **5b**(*S*): *Rf* 0.25 (hexane: ethyl acetate=9: 1). IR $\nu_{max}^{neat}$ $cm^{-1}$: 1740, 1720, 1440, 1360, 1255, 1100, 975, 840, 780. NMR ($CCl_4$) $\delta$: 0.02 (6H, s, $SiMe_2$), 0.86 (9H, s, $^t$Bu), 0.9—1.9 (13H, m), 2.0—2.4 (9H, m), 1.97 (3H, s, $COCH_3$), 3.57 (3H, s, $COOCH_3$), 3.67 (1H, m, $C_{12}H$), 5.2—5.4 (4H, m, olefinic H). **6b**(*S*); *Rf* 0.35 (hexane: ethyl acetate=9: 1). IR $\nu_{max}^{neat}$ $cm^{-1}$: 1740, 1720, 1440, 1360, 1250, 1095, 965, 840, 780. NMR ($CCl_4$) $\delta$: 0.02 (6H, s, $SiMe_2$), 0.83 (9H, s, $^t$Bu), 0.9—1.9

(13H, m), 1.9—2.4 (12H, m), 3.51 (3H, s, $COOCH_3$), 3.69 (1H, m, $C_{14}H$), 5.2—5.7 (4H, m, olefinic H).

(c) Methyl (5*Z*,10*E*)-(8*RS*,12*S*)-8-Acetyl-12-cyclohexyl-12-hydroxy-5,10-dodecadienoate (**7b**(*S*)): In a similar manner, acidic hydrolysis of **5b**(*S*) (41 mg, 0.088 mmol) yielded **7b**(*S*) (21 mg, 0.060 mmol, 68.2%). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3490, 1735, 1710, 1440, 1360, 1165, 1005, 975. NMR ($CCl_4$) $\delta$: 0.8—2.5 (22H, m), 1.99 (3H, s, $COCH_3$), 3.56 (3H, s, $COOCH_3$), 3.63 (1H, m, $C_{12}H$), 5.17—5.5 (4H, m, olefinic H). MS (20 eV) *m/e*: 350 ($M^+$), 332 ($M-H_2O$). High-resolution MS for $C_{21}H_{32}O_3$ (dehydration peak from molecular ion): Calcd *m/e*: 332.2353; Found: 332.2366.

(d) (5*Z*,10*E*)-(8*RS*,12*S*)-8-Acetyl-12-cyclohexyl-12-hydroxy-5,10-dodecadienoic Acid (**9b**(*S*)): Similar saponification of **7b**(*S*) (21 mg, 0.06 mmol) afforded **9b**(*S*) (17 mg, 0.051 mmol, 84.3%). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3300, 1720. NMR ($CDCl_3$) $\delta$: 0.9—2.5 (22H, m), 2.04 (3H, s, $COCH_3$), 3.73 (1H, m, $C_{12}H$), 5.2—5.55 (4H, m, olefinic H), 5.9 (2H, bs, OH and COOH).

**(5*Z*,10*E*)-(8*RS*,12*R*)-8-Acetyl-12-cyclohexyl-12-hydroxy-5,10-dodecadienoic Acid (9b(*R*)) and (5*Z*,12*E*)-(14*R*)-14-Cyclohexyl-14-hydroxy-9-oxo-5,12-tetradecadienoic Acid (10b(*R*))**——(a) (5*E*)-(7*R*)-7-*tert*-Butyldimethylsilyloxy-7-cyclohexyl-5-hepten-2-one (**3b**(*R*)): (1*E*)-(3*R*)-3-*tert*-Butyldimethylsilyloxy-3-cyclohexyl-1-iodo-1-propene (**1b**(*R*); $[\alpha]_D^{18}$ +26.7° (*c*=3.81, $CCl_4$)) was similarly prepared from (−)-(1*E*)-(3*R*)-3-cyclohexyl-3-hydroxy-1-iodo-1-propene which had been resolved with (+)-α-methylbenzylamine. Similar conjugate addition of **2b**(*R*) to methyl vinyl ketone gave **3b**(*R*) in 30.3% yield. IR $\nu_{max}^{neat}$ $cm^{-1}$: 1720, 1670, 1450, 1360, 1255, 1095, 1050, 835, 775. NMR ($CDCl_3$) $\delta$: 0.08 (6H, s, $SiMe_2$), 0.84 (9H, s, $^t$Bu), 0.9—1.9 (11H, m), 2.08 (3H, s, $COCH_3$), 2.15—2.55 (4H, m, $C_3H_2$ and $C_4H_2$), 3.67 (1H, m, $C_7H$), 5.3—5.5 (2H, olefinic H).

(b) Methyl (5*Z*,10*E*)-(8*RS*,12*R*)-8-Acetyl-12-*tert*-butyldimethylsilyloxy-12-cyclohexyl-5,10-dodecadienoate (**5b**(*R*)) and Methyl (5*Z*,12*E*)-(14*R*)-14-*tert*-Butyldimethylsilyloxy-14-cyclohexyl-9-oxo-5,12-tetradecadienoate (**6b**(*R*)): Reaction of **3b**(*R*) (162 mg, 0.5 mmol) and **4g** (162 mg, 0.6 mmol) by method A gave **5b**(*R*) (54 mg, 0.116 mmol, 23.3%) and **6b**(*R*) (22 mg, 0.047 mmol, 9.5%). **5b**(*R*); *Rf* 0.25 (hexane: ethyl acetate=9: 1). IR $\nu_{max}^{neat}$ $cm^{-1}$: 1740, 1720, 1440, 1360, 1255, 1100, 980, 840, 780. NMR ($CCl_4$) $\delta$: 0.03 (6H, s, $SiMe_2$), 0.89 (9H, s, $^t$Bu), 0.9—2.0 (13H, m), 2.0—2.5 (9H, m), 2.04 (3H, s, $COCH_3$), 3.63 (3H, s, $COOCH_3$), 3.73 (1H, m, $C_{12}H$), 5.2—5.5 (4H, m, olefinic H). **6b**(*R*); *Rf* 0.35 (hexane: ethyl acetate=9: 1). IR $\nu_{max}^{neat}$ $cm^{-1}$: 1740, 1720, 1440, 1255, 1100, 970, 840, 780. NMR ($CCl_4$) $\delta$: 0.01 (6H, s, $SiMe_2$), 0.84 (9H, s, $^t$Bu), 0.9—1.9 (13H, m), 1.9—2.4 (12H, m), 3.56 (3H, s, $COOCH_3$), 3.60 (1H, m, $C_{14}H$), 5.2—5.5 (4H, m, olefinic H).

(c) Methyl (5*Z*,10*E*)-(8*RS*,12*R*)-8-Acetyl-12-cyclohexyl-12-hydroxy-5,10-dodecadienoate (**7b**(*R*)) and Methyl (5*Z*,12*E*)-(14*R*)-14-Cyclohexyl-14-hydroxy-9-oxo-5,12-tetradecadienoate (**8b**(*R*)): Similar acidic desilylation of **5b**(*R*) (54 mg, 0.116 mmol) and **6b**(*R*) (22 mg, 0.047 mmol) gave **7b**(*R*) (35 mg, 0.100 mmol, 86.2%) and **8b**(*R*) (13 mg, 0.037 mmol, 79%), respectively. **7b**(*R*); IR $\nu_{max}^{neat}$ $cm^{-1}$: 3480, 1740, 1710, 1445, 1435, 1360, 1240, 1200, 1165, 1000, 970. NMR ($CCl_4$) $\delta$: 0.9—2.3 (22H, m), 1.99 (3H, s, $COCH_3$), 3.56 (3H, s, $COOCH_3$), 3.63 (1H, m, $C_{12}H$), 5.2—5.5 (4H, m, olefinic H). MS (20 eV) *m/e*: 350 ($M^+$), 332 ($M-H_2O$). High-resolution MS for $C_{21}H_{32}O_3$ (dehydration peak from molecular ion): Calcd *m/e*: 332.2353; Found: 332.2344. **8b**(*R*); IR $\nu_{max}^{neat}$ $cm^{-1}$: 3430, 1740, 1720, 1455, 1440, 1255, 1175, 1010, 980. NMR ($CCl_4$) $\delta$: 0.85—1.9 (13H, m), 1.9—2.6 (12H, m), 3.56 (3H, s, $COOCH_3$), 3.63 (1H, m, $C_{14}H$), 5.2—5.5 (4H, m, olefinic H). MS (20 eV) *m/e*: 350 ($M^+$), 332 ($M-H_2O$). High-resolution MS for $C_{21}H_{32}O_3$ (dehydration peak from molecular ion): Calcd *m/e*: 332.2353; Found 332.2379.

(d) (5*Z*,10*E*)-(8*RS*,12*R*)-8-Acetyl-12-cyclohexyl-12-hydroxy-5,10-dodecadienoic Acid (**9b**(*R*)) and (5*Z*,12*E*)-(14*R*)-14-Cyclohexyl-14-hydroxy-9-oxo-5,12-tetradecadienoic Acid (**10b**(*R*)): **7b**(*R*) (35 mg, 0.100 mmol) and **8b**(*R*) (13 mg, 0.037 mmol) were similarly hydrolyzed with NaOH to yield **9b**(*R*) (25 mg, 0.074 mmol, 74.4%) and **10b**(*R*) (10 mg, 0.030 mmol, 80.5%), respectively. **9b**(*R*); IR $\nu_{max}^{neat}$ $cm^{-1}$: 3300, 1720. NMR ($CDCl_3$) $\delta$: 0.8—2.5 (22H, m), 2.04 (3H, s, $COCH_3$), 3.70 (1H, m, $C_{12}H$), 5.2—5.5 (4H, m, olefinic H), 6.06 (2H, bs, OH and COOH). **10b**(*R*); IR $\nu_{max}^{neat}$ $cm^{-1}$: 3200, 1710. NMR ($CDCl_3$) $\delta$: 0.8—2.0 (13H, m), 2.1—2.5 (12H, m), 3.8 (1H, m, $C_{14}H$), 4.8 (2H, bs, OH and COOH), 5.2—5.6 (4H, m, olefinic H).

**(5*Z*,10*E*)-(8*RS*,12*RS*)-8-Acetyl-12-hydroxy-12-methyl-5,10-heptadecadienoic acid (*dl*-9c) and (5*Z*,12*E*)-(14*RS*)-14-Hydroxy-14-methyl-9-oxo-5,12-nonadecadienoic Acid (*dl*-10c)**——(a) (5*E*)-(7*RS*)-7-*tert*-Butyldimethylsilyloxy-7-methyl-5-dodecen-2-one (*dl*-**3c**): (1*E*)-(3*RS*)-3-*tert*-Butyldimethylsilyloxy-1-iodo-3-methyl-1-octene (*dl*-**1c**) was obtained through Grignard methylation of (1*E*)-1-iodo-1-octen-3-one.[12] Similar conjugate addition of the cuprate (*dl*-**2c**) formed from *dl*-**1c** to methyl vinyl ketone provided *dl*-**3c** in 15.3% yield. IR $\nu_{max}^{neat}$ $cm^{-1}$: 1710. NMR ($CCl_4$) $\delta$: 0.08 (6H, bs, $SiMe_2$), 0.90 (12H, bs, $^t$Bu and $C_{12}H_3$), 1.23 (3H, s, $C_7Me$), 0.9—1.8 (10H, m), 2.03 (3H, s, $COCH_3$), 1.8—2.5 (4H, m, $C_3H_2$ and $C_4H_2$), 5.5 (2H, m, olefinic H). MS *m/e*: 311 (M−Me), 269 (M−57).

(b) Methyl (5*Z*,10*E*)-(8*RS*,12*RS*)-8-Acetyl-12-*tert*-butyldimethylsilyloxy-12-methyl-5,10-heptadecadienoate (*dl*-**5c**) and Methyl (5*Z*,12*E*)-(14*RS*)-14-*tert*-Butyldimethylsilyloxy-14-methyl-9-oxo-5,12-nonadecadienoate (*dl*-**6c**): *dl*-**3c** (100 mg, 0.31 mmol) was similarly alkylated with **4h** (88 mg, 0.40 mmol) by method B to give *dl*-**5c** (66 mg, 0.14 mmol, 45.2%) and *dl*-**6c** (37 mg, 0.08 mmol, 25.8%). *dl*-**5c**; IR $\nu_{max}^{neat}$ $cm^{-1}$: 1740, 1710. NMR ($CCl_4$) $\delta$: 0.08 (6H, bs, $SiMe_2$), 0.90 (12H, bs, $^t$Bu and $C_{17}H_3$), 1.0—1.3 (10H, m), 1.26 (3H, s, $C_{12}Me$), 1.7—2.4 (9H, m), 2.06 (3H, s, $COCH_3$), 3.64 (3H, s, $COOCH_3$), 5.44 (4H, m, olefinic H). MS *m/e*: 451 (M−Me), 409 (M−57). *dl*-**6c**; IR $\nu_{max}^{neat}$ $cm^{-1}$: 1740, 1710. NMR ($CCl_4$) $\delta$: 0.08 (6H, bs, $SiMe_2$), 0.90 (12H, bs, $^t$Bu and $C_{19}H_3$), 1.1—1.5 (10H, m), 1.26 (3H, s, $C_{12}Me$), 1.9—2.4 (12H, m), 3.62 (3H, s, $COOCH_3$), 5.47 (4H, m, olefinic H). MS *m/e*: 451 (M−Me), 409 (M−57).

(c) Methyl (5*Z*,10*E*)-(8*RS*,12*RS*)-8-Acetyl-12-hydroxy-12-methyl-5,10-heptadecadienorate (*dl*-**7c**) and Methyl (5*Z*,10*E*)-(14*RS*)-14-Hydroxy-14-methyl-9-oxo-5,12-nonadecadienoate (*dl*-**8c**): Similar acidic desilylation of *dl*-**5c** (66 mg, 0.14 mmol) and *dl*-**6c** (37 mg, 0.08 mmol) provided *dl*-**7c** (13 mg, 0.037 mmol, 26.4%) and *dl*-**8c** (11 mg, 0.031 mmol, 39.1%), respectively. *dl*-**7c**; IR $\nu_{max}^{neat}$ cm$^{-1}$: 3460, 1735, 1710. NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J$=7 Hz, $C_{17}H_3$), 1.1—1.4 (10H, m), 1.20 (3H, s, $C_{12}Me$), 1.8—2.3 (9H, m), 2.06 (3H, s, $COCH_3$), 3.62 (3H, s, $COOCH_3$), 5.1—5.5 (4H, m, olefinic H). High-resolution MS for $C_{21}H_{36}O_4$ (molecular ion): Calcd *m/e*: 352.2616; Found: 352.2648. *dl*-**8c**; IR $\nu_{max}^{neat}$ cm$^{-1}$: 3460, 1735, 1710. NMR ($CDCl_3$) $\delta$: 0.84 (3H, t, $J$=7 Hz, $C_{19}H_3$), 1.0—1.4 (10H, m), 1.20 (3H, s, $C_{14}Me$), 1.5—2.5 (12H, m), 3.60 (3H, s, $COOCH_3$), 5.0—5.5 (4H, m, olefinic H). High-resolution MS for $C_{21}H_{34}O_3$ (dehydration peak from molecular ion): Calcd *m/e*: 334.2510; Found: 334.2438.

(d) (5*Z*,10*E*)-(8*RS*,12*RS*)-8-Acetyl-12-hydroxy-12-methyl-5,10-heptadecadienoic Acid (*dl*-**9c**) and (5*Z*,12*E*)-(14*RS*)-14-Hydroxy-14-methyl-9-oxo-5,12-nonadecadienoic Acid (*dl*-**10c**): Saponification of *dl*-**7c** (13 mg, 0.037 mmol) and *dl*-**8c** (11 mg, 0.031 mmol) with NaOH gave the sodium salts of *dl*-**9c** and *dl*-**10c**, respectively.

**(5*Z*,10*E*)-(8*RS*)-8-Acetylheptadeca-5,10-dienoic Acid (9d) and (5*Z*,12*E*)-9-Oxo-5,12-nonadecadienoic Acid (10d)**——(a) (5*E*)-5-Dodecaen-2-one (**3d**): Conjugate addition of the cuprate (**2d**) prepared from **1d** was carried out as described for **3a**(*S*), and **3d** was obtained in 13% yield. IR $\nu_{max}^{neat}$ cm$^{-1}$: 1715. NMR ($CDCl_3$) $\delta$: 0.86 (3H, t, $J$=5 Hz, $C_{12}H_3$), 1.05—1.6 (8H, m), 2.10 (3H, s, $COCH_3$), 1.7—2.6 (6H, m), 5.39 (2H, m, olefinic H).

(b) Methyl (5*Z*,10*E*)-(8*RS*)-8-Acetyl-5,10-heptadecadienoate (**5d**) and Methyl (5*Z*,12*E*)-9-Oxo-5,12-nonadecadienoate (**6d**): Using method B, **3d** (250 mg, 1.37 mmol) was alkylated with **4h** (394 mg, 1.78 mmol) to give **5d** (93 mg, 0.29 mmol, 21.2%) and **6d** (24 mg, 0.075 mmol, 5.4%). **5d**: IR $\nu_{max}^{neat}$ cm$^{-1}$: 1740, 1710, 965. NMR ($CDCl_3$) $\delta$: 0.86 (3H, t, $J$=5 Hz, $C_{17}H_3$), 2.08 (3H, s, $COCH_3$), 1.05—2.7 (21H, m), 3.64 (3H, s, $COOCH_3$), 5.35 (4H, m, olefinic H). High-resolution MS for $C_{20}H_{34}O_3$ (molecular ion): Calcd *m/e*: 322.2510; Found: 322.2564. **6d**; IR $\nu_{max}^{neat}$ cm$^{-1}$: 1740, 1710, 965. NMR ($CDCl_3$) $\delta$: 0.86 (3H, t, $J$=5 Hz, $C_{19}H_3$), 1.0—2.7 (24H, m), 3.63 (3H, s, $COOCH_3$), 5.35 (4H, m, olefinic H). High-resolution MS for $C_{20}H_{34}O_3$ (molecular ion): Calcd *m/e*: 322.2510; Found: 322.2481.

(c) (5*Z*,10*E*)-(8*RS*)-8-Acetyl-5,10-heptadecadienoic Acid (**9d**) and (5*Z*,12*E*)-9-Oxo-5,12-nonadecadienoic Acid (**10d**): **5d** (73 mg, 0.23 mmol) and **6d** (22 mg, 0.068 mmol) were analogously hydrolyzed with NaOH to give **9d** (49 mg, 0.16 mmol, 69%) and **10d** (19 mg, 0.062 mmol, 91%), respectively. **9d**: IR $\nu_{max}^{neat}$ cm$^{-1}$: 3600—2400, 1708, 965. NMR ($CDCl_3$) $\delta$: 0.86 (3H, bt, $J$=5 Hz, $C_{17}H_3$), 2.07 (3H, s, $COCH_3$), 1.0—2.7 (21H, m), 5.34 (4H, m, olefinic H), 9.07 (1H, bs, COOH). **10d**; IR $\nu_{max}^{neat}$ cm$^{-1}$: 3600—2400, 1708, 965. NMR ($CDCl_3$) $\delta$: 0.86 (3H, bt, $J$=5 Hz, $C_{19}H_3$), 1.0—2.7 (24H, m), 5.35 (4H, m, olefinic H), 7.55 (1H, bs,COOH).

**(10*E*)-(8*RS*,12*S*)-8-Acetyl-12-hydroxy-10-heptadecen-5-ynoic Acid (9a′(*S*))**——(a) Methyl (10*E*)-(8*RS*,12*S*)-8-Acetyl-12-*tert*-butyldimethylsilyloxy-10-heptadecen-5-ynoate (**5a**′(*S*)): Similar alkylation of **3a**(*S*) (245 mg, 0.785 mmol) with bromide (**4i**; 223 mg, 1.02 mmol) using method B yielded **5a**′(*S*) (20 mg, 0.044 mmol, 5.7%). IR $\nu_{max}^{neat}$ cm$^{-1}$: 1740, 1710. NMR ($CDCl_3$) $\delta$: 0.07 (6H, s, $SiMe_2$), 0.86 (12H, bs, $^t$Bu and $C_{17}H_3$), 1.2—1.4 (10H, m), 2.13 (3H, s, $COCH_3$), 2.1—2.7 (9H, m), 3.66 (3H, s, $COOCH_3$), 3.75—4.2 (1H, m, $C_{12}H$), 5.25—5.65 (2H, m, olefinic H).

(b) Methyl (10*E*)-(8*RS*,12*S*)-8-Acetyl-12-hydroxy-10-heptadecen-5-ynoate (**7a**′(*S*)): Desilylation of **5a**′(*S*) (15 mg, 0.033 mmol) under acidic conditions gave **7a**′(*S*) (11 mg, 0.033 mmol, 93%). IR $\nu_{max}^{neat}$ cm$^{-1}$: 3450, 1740, 1710, 965. NMR ($CDCl_3$) $\delta$: 0.89 (3H, m, $C_{17}H_3$), 1.0—1.5 (10H, m), 2.17 (3H, s, $COCH_3$), 2.1—2.6 (9H, m), 3.68 (3H, s, $COOCH_3$), 3.7—4.2 (1H, bs, $C_{12}H$), 5.49 (2H, m, olefinic H). MS *m/e*: 318 (M−$H_2O$), 287, 275. High-resolution MS for $C_{20}H_{30}O_3$ (dehydration peak from molecular ion): Calcd *m/e*: 318.2197; Found: 318.2174.

(c) (10*E*)-(8*RS*,12*S*)-8-Acetyl-12-hydroxy-10-heptadecen-5-ynoic Acid (**9a**′(*S*)): Alkaline hydrolysis of **7a**′(*S*) (11 mg, 0.033 mmol) yielded **9a**′(*S*) (8 mg, 0.025 mmol, 76%). IR $\nu_{max}^{neat}$ cm$^{-1}$: 3700—2200, 1710, 965. NMR ($CDCl_3$) $\delta$: 0.86 (3H, m, $C_{17}H_3$), 1.15—1.6 (10H, m), 2.16 (3H, s, $COCH_3$), 2.2—2.8 (9H, m), 4.16 (1H, bs, $C_{12}H$), 5.40 (2H, bs, OH and COOH, disappeared with $D_2O$), 5.4—5.6 (2H, m, olefinic H).

**(5*Z*,10*E*)-(8*RS*,9*RS*,12*S*)-8-Acetyl-12-hydroxy-9-methyl-5,10-heptadecadienoic Acid (16e)**——(a) (5*E*)-(4*RS*,9*S*)-7-*tert*-Butyldimethylsilyloxy-4-methyl-5-dodecen-2-one (**12e**): Conjugate addition of cuprate (**2a**(*S*)) to crotyl methyl ketone (**11e**) was carried out as described for **3a**(*S*). A similar work-up and separation gave **12e** in 65% yield. IR $\nu_{max}^{neat}$ cm$^{-1}$: 1715, 965. NMR ($CDCl_3$) $\delta$: 0.07 (6H, s, $SiMe_2$), 0.95 (12H, bs, $^t$Bu and $C_{12}H_3$), 0.98 (3H, d, $J$=6 Hz, $C_4Me$), 1.05—1.7 (8H, m), 2.06 (3H, s, $COCH_3$), 2.16—2.9 (3H, m, $C_3H_2$ and $C_4H$), 3.95 (1H, m, $C_7H$), 5.40 (2H, m, olefinic H). MS *m/e*: 311 (M−Me), 269, 255, 211.

(b) Methyl (5*Z*,10*E*)-(8*RS*,9*RS*,12*S*)-8-Acetyl-12-*tert*-butyldimethylsilyloxy-9-methyl-5,10-heptadecadienoate (**13e**) and Methyl (5*Z*,12*E*)-(11*RS*,14*S*)-14-*tert*-Butyldimethylsilyloxy-11-methyl-9-oxo-5,12-nonadecadienoate (**14e**): The above ester (**12e**; 186 mg, 0.57 mmol) was alkylated with bromide (**4h**; 150 mg, 0.68 mmol) using method B to give **13e** (45 mg, 0.097 mmol, 17%) and **14e** (13 mg, 0.028 mmol, 5%). **13e**: IR $\nu_{max}^{neat}$ cm$^{-1}$: 1740, 1710, 965. NMR ($CDCl_3$) $\delta$: 0.06 (6H, s, $SiMe_2$), 0.86 (15H, bs, $^t$Bu, $C_9Me$, and $C_{17}H_3$), 1.0—1.7 (10H, m), 2.00 (3H, s, $COCH_3$), 1.7—2.5 (8H, m), 3.60 (3H, s, $COOCH_3$), 3.70—4.20 (1H, m, $C_{12}H$), 5.10—5.40 (4H, m, olefinic H). **14e**; IR $\nu_{max}^{neat}$ cm$^{-1}$: 1740, 1710, 970. NMR ($CDCl_3$) $\delta$: 0.08 (6H, s, $SiMe_2$), 0.86 (12H, bs, $^t$Bu and $C_{19}H_3$), 0.98 (3H, d, $J$=6 Hz, $C_{11}Me$), 1.0—1.7 (10H, m), 1.7—2.6 (11H, m), 3.60

(3H, s, $COOCH_3$), 3.95 (1H, m, $C_{14}H$), 5.3 (4H, m, olefinic H).

(c) Methyl (5*Z*,10*E*)-(8*RS*,9*RS*,12*S*)-8-Acetyl-12-hydroxy-9-methyl-5,10-heptadecadienoate (**15e**): Hydrolysis of **13e** (53 mg, 0.114 mmol) with aqueous acetic acid gave the corresponding hydroxy ester (**15e**; 30 mg, 0.085 mmol, 75%). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3450, 1740, 1710. NMR ($CDCl_3$) $\delta$: 0.95 (6H, m, $C_9Me$ and $C_{17}H_3$), 1.05—1.7 (10H, m), 2.03 (3H, s, $COCH_3$), 1.7—2.5 (9H, m), 3.60 (3H, s, $COOCH_3$), 3.96 (1H, m, $C_{12}H$), 5.30 (4H, m, olefinic H). MS (20 eV) *m/e*: 352 ($M^+$), 334. High-resolution MS for $C_{21}H_{34}O_3$ (dehydration peak from molecular ion); Calcd *m/e*: 334.2510; Found: 334.2502.

(d) (5*Z*,10*E*)-(8*RS*,9*RS*,12*S*)-8-Acetyl-12-hydroxy-9-methyl-5,10-heptadecadienoic Acid (**16e**): The above ester (**15e**; 30 mg, 0.085 mmol) was similarly converted by alkaline saponification into **16e** (28 mg, 0.082 mmol, 97%). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3400, 1710. NMR ($CDCl_3$) $\delta$: 0.9 (6H, m, $C_9Me$ and $C_{17}H_3$), 1.06—1.7 (10H, m), 1.7—2.5 (8H, m), 1.98 and 2.02 (3H, 2s, diastereomeric $COCH_3$), 3.98 (1H, m, $C_{12}H$), 5.30 (4H, m, olefinic H), 5.55 (2H, bs, OH and COOH).

**(5*Z*,10*E*)-(8*RS*,12*S*)-12-Hydroxy-8-propionyl-5,10-heptadecadienoic Acid (16f)**——(a) (6*E*)-(8*S*)-8-*tert*-Butyldimethylsilyloxy-6-tridecen-3-one (**12f**): The ketone **12f** was prepared in 19% yield from cuprate (**2a**(*S*)) and ethyl vinyl ketone (**11f**) by the same method as applied for the preparation of **3a**(*S*). **12f**; IR $\nu_{max}^{neat}$ $cm^{-1}$: 1720, 965. NMR ($CDCl_3$) $\delta$: 0.08 (6H, s, $SiMe_2$), 0.85 (12H, s, $^t$Bu and $C_{13}H_3$), 1.06 (3H, t, $J$= 7 Hz, $C_1H_3$), 1.1—1.7 (8H, m), 2.1—2.7 (6H, m), 3.95 (1H, m, $C_8H$), 5.45 (2H, m, olefinic H).

(b) Methyl (5*Z*,10*E*)-(8*RS*,12*S*)-12-*tert*-Butyldimethylsilyloxy-8-propionyl-5,10-heptadecadienoate (**13f**): Similar alkylation by method A of the above ketone (**12f**; 113 mg, 0.347 mmol) with iodide (**4g**; 112 mg, 0.400 mmol) yielded **13f** (87 mg, 0.182 mmol, 52.5%). IR $\nu_{max}^{neat}$ $cm^{-1}$: 1740, 1710. NMR ($CDCl_3$) $\delta$: 0.08 (6H, s, $SiMe_2$), 0.8—1.0 (15H, m, $^t$Bu, $C_{17}H_3$, and $C_3'H_3$), 1.15—1.65 (10H, m), 1.65—2.65 (11H, m), 3.63 (3H, s, $COOCH_3$), 4.00 (1H, m, $C_{12}H$), 5.2—5.55 (4H, m, olefinic H).

(c) Methyl (5*Z*,10*E*)-(8*RS*,12*S*)-12-Hydroxy-8-propionyl-5,10-heptadecadienoate (**15f**): Subsequent desilylation of **13f** (87 mg, 0.182 mmol) and purification gave **15f** (38 mg, 0.108 mmol, 59.3%). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3450, 1735, 1705, 965. NMR ($CDCl_3$) $\delta$: 0.09 (6H, s, $SiMe_2$), 0.93 (3H, m, $C_{17}H_3$), 0.97 (3H, t, $J$=6 Hz, $C_3'H_3$), 1.05—2.65 (22H, m), 3.60 (3H, s, $COOCH_3$), 3.80—4.20 (1H, m, $C_{12}H$), 5.30 (4H, m, olefinic H). MS *m/e*: 352 ($M^+$), 334, 303, 277, 263. High-resolution MS for $C_{21}H_{34}O_3$ (dehydration peak from molecular ion): Calcd *m/e*: 334.2510; Found: 334.2478.

(d) (5*Z*,10*E*)-(8*RS*,12*S*)-12-Hydroxy-8-propionyl-5,10-heptadecadienoic Acid (**16f**): The ester (**15f**; 38 mg, 0.108 mmol) was similarly saponified with aqueous NaOH to afford **16f** (20 mg, 0.059 mmol, 54.8%). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3400, 1710, 965. NMR ($CDCl_3$) $\delta$: 0.75—1.1 (6H, m, $C_{17}H_3$ and $C_3'H_3$), 1.1—1.4 (10H, m), 1.8—2.6 (11H, m), 4.00 (1H, m, $C_{12}H$), 4.93 (2H, bs, OH and COOH), 5.2—5.6 (4H, m, olefinic H).

**(5*Z*,10*E*)-(8*RS*,12*S*)-12-Hydroxy-8-((*RS*)-1-hydroxyethyl)-5,10-heptadecadienoic Acid (20)**——(a) Methyl (5*Z*,10*E*)-(8*RS*,12*S*)-12-*tert*-Butyldimethylsilyloxy-8-((*RS*)-1-hydroxyethyl)-5,10-heptadecadienoate (**18**): Powdered $NaBH_4$ (6 mg, 0.158 mmol) was added at room temperature to a stirred solution of **5a**(*S*) (15 mg, 0.033 mmol), and the mixture was stirred for 1 h. After removal of the MeOH, AcOEt (15 ml) was added to the residue. The organic layer was washed with saturated $NH_4Cl$ (4×5 ml), dried ($MgSO_4$), and concentrated. The resulting oil was purified by preparative TLC (cyclohexane: ethyl acetate=7: 3) to yield **18** (13 mg, 0.029 mmol, 88%). *Rf* 0.40 (cyclohexane: ethyl acetate=7: 3). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3300, 1740. NMR ($CDCl_3$) $\delta$: 0.08 (6H, s, $SiMe_2$), 0.87 (9H, s, $^t$Bu), 0.90 (3H, t, $J$=7 Hz, $C_{17}H_3$), 1.15 (3H, d, $J$=6 Hz, $C_2'H_3$), 1.1—1.8 (11H, m), 1.8—2.45 (8H, m), 3.60 (3H, s, $COOCH_3$), 3.6—4.2 (2H, m, $C_1'H$ and $C_{12}H$), 5.2—5.6 (4H, m, olefinic H). MS *m/e*: 397 (M−57).

(b) Methyl (5*Z*,10*E*)-(8*RS*,12*S*)-12-Hydroxy-8-((*RS*)-1-hydroxyethyl)-5,10-heptadecadienoate (**19**): Usual desilylation of **18** (13 mg, 0.029 mmol) with a solution of $CH_3COOH$ (0.5 ml), $H_2O$ (0.2 ml), and THF (0.2 ml) gave **19** (8.5 mg, 0.025 mmol, 86%). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3400, 1735, 965. NMR ($CDCl_3$) $\delta$: 0.90 (3H, t, $J$=7 Hz, $C_{17}H_3$), 1.13 (3H, d, $J$=7 Hz, $C_2'H_3$), 1.1—1.8 (11H, m), 1.8—2.5 (8H, m), 3.67 (3H, s, $COOCH_3$), 3.6—4.2 (2H, m, $C_1'H$ and $C_{12}H$), 5.2—5.6 (4H, m, olefinic H). MS (trimethylsilylated **19**) *m/e*: 484 ($M^+$), 469 (M−Me), 413, 394. The diol (**19**) was alternatively prepared by $NaBH_4$ reduction of the hydroxy ketone (**7a**(*S*); 46 mg, 0.136 mmol) in 86% (40 mg, 0.118 mmol) yield.

(c) (5*Z*,10*E*)-(8*RS*,12*S*)-12-Hydroxy-8-((*RS*)-1-hydroxyethyl)-5,10-heptadecadienoic Acid (**20**): The diol ester (**19**; 8 mg, 0.024 mmol) was likewise saponified to provide **20** (5 mg, 0.015 mmol, 64%). IR $\nu_{max}^{neat}$ $cm^{-1}$: 3600—2400, 1710, 970. NMR ($CDCl_3$) $\delta$: 0.88 (3H, t, $J$=6 Hz, $C_{17}H_3$), 1.13 (3H, d, $J$=6 Hz, $C_2H_3$), 1.1—1.6 (11H, m), 1.8—2.5 (8H, m), 3.7—4.2 (2H, m, $C_1'H$ and $C_{12}H$), 4.32 (3H, m, OH and COOH), 5.32—5.70 (4H, m, olefinic H).

**Methyl (10*E*)-(8*RS*,12*S*)-8-Acetyl-12-hydroxy-6-oxo-10-heptadecenoate (24)**——(a) (1*RS*,2*RS*,4*RS*)-2-[(2*E*)-(4*S*)-4-*tert*-Butyldimethylsilyloxy-2-nonen-1-yl]-4-((1*RS*)-4-methoxycarbonyl-1-iodobutyl)-1-methyltetrahydrofuran (**21**): A stirred suspension of **18** (66 mg, 0.145 mmol) and $K_2CO_3$ (40 mg, 0.290 mmol) in $CH_2Cl_2$ (1 ml) was treated at −15°C with a solution of iodine (44 mg, 0.174 mmol) in $CH_2Cl_2$ (2 ml), and the mixture was stirred at −15——20°C for 4.5 h. After standing at −20°C for 20 h, the mixture was diluted with $CH_2Cl_2$ (20 ml), then washed with aqueous 10% $Na_2SO_3$ (0.5 ml) and brine (3×5 ml). The separated organic layer was dried over $MgSO_4$, and concentrated *in vacuo* to give 76 mg of an oily residue. Purification by preparative TLC (cyclohexane: ethyl acetate=9: 1) yielded **21** (50 mg, 0.086 mmol, 59%) as a viscous oil showing one spot on TLC (*Rf* 0.33, cyclohexane: ethyl acetate=9: 1). NMR ($CDCl_3$) $\delta$: 0.07 (6H, s,

$SiMe_2$), 0.88 (12H, bs, $^tBu$ and terminal Me), 1.20 (3H, d, $J$=6 Hz, $C_1Me$), 1.05—2.55 (19H, m), 3.66 (3H, s, $COOCH_3$), 3.45—4.3 (4H, m), 5.3—5.6 (2H, m, olefinic H).

(b) Methyl (10*E*)-(8*RS*,12*S*)-12-*tert*-Butyldimethylsilyloxy-8-((*RS*)-1-hydroxyethyl)-6-oxo-10-heptadecenoate (**22**): A mixture of iodide (**21**; 50 mg, 0.086 mmol) and DBN (45 mg, 0.36 mmol) in benzene (10 ml) was heated under reflux for 18 h. The mixture was diluted with ether (20 ml), washed with water (4×5 ml), and dried over $K_2CO_3$–$MgSO_4$. Removal of the solvents by evaporation left a crude olefinic product, which was then subjected to desilylation by dissolving it in a mixture of $CH_3COOH$ (0.5 ml), $H_2O$ (0.1 ml), and THF (1 ml). After being stirred at room temperature for 10 min, the solution was diluted with ether (30 ml), then washed with saturated $NaHCO_3$ (4×10 ml) and brine (2×5 ml). The separated aqueous layer was extracted once with ether (10 ml). The combined organic layer was dried over $Na_2SO_4$ and concentrated *in vacuo* to leave 42 mg of an oily residue. Separation by preparative TLC (cyclohexane: ethyl acetate=7: 3) gave two diastereometric products, **22**. Less polar **22** (15.5 mg, 0.033 mmol, 38.3%). *Rf* 0.25 (cyclohexane: ethyl acetate=7: 3). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3400, 1740, 965. NMR ($CDCl_3$) $\delta$: 0.08 (6H, s, $SiMe_2$), 0.88 (12H, bs, $^tBu$ and $C_{17}H_3$), 1.0—2.5 (22H, m), 3.68 (3H, s, $COOCH_3$), 3.7—4.2 (2H, m, $C_1'H$ and $C_{12}H$), 5.32—5.60 (2H, m, olefinic H). MS (after trimethylsilylation) *m/e*: 527 (M−15) 485 (M−57), 395. More polar **22** (9 mg, 0.019 mmol, 22.2%). *Rf* 0.20 (the same solvent system). The more polar **22** was essentially identical (IR, NMR and MS) with the former **22**. Thus, these two components are diastereoisomers probably based on the 8-(1-hydroxyethyl) and 12(*S*)-silyloxy groups, as shown in the following experiments (*vide infra*).

(c) Methyl (10*E*)-(8*RS*,12*S*)-8-Acetyl-12-*tert*-butyldimethylsilyloxy-6-oxo-10-heptadecenoate (**23**): A solution of the above more polar **22** (9 mg, 0.019 mmol) in $CH_2Cl_2$ (0.2 ml) was added at room temperature to a mixture of $CrO_3$ (12.3 mg, 0.123 mmol) and pyridine (19.5 mg, 0.246 mmol) in $CH_2Cl_2$ (0.3 ml), and the mixture was stirred for 25 min. The mixture was diluted with ether (10 ml) and filtered through celite. The filtrate was washed with aqueous $NH_4Cl$ and brine, dried over $MgSO_4$, and concentrated to give **23** (8 mg, 0.017 mmol, 89%), which showed essentially a single spot on TLC (*Rf* 0.35, cyclohexane: ethyl acetate =7: 3). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 1740, 1717, 965. NMR ($CDCl_3$) $\delta$: 0.06 (6H, s, $SiMe_2$), 0.86 (12H, bs, $^tBu$ and $C_{17}H_3$), 1.0—2.0 (12H, m), 2.0—3.1 (9H, m), 2.20 (3H, s, $COCH_3$), 3.63 (3H, s, $COOCH_3$), 3.9—4.2 (1H, m, $C_{12}H$), 5.48 (2H, m, olefinic H). A similar oxidation of the less polar **22** gave **23** showing the same TLC behavior and spectra (IR, NMR, MS) in 80% yield.

(d) Methyl (10*E*)-(8*RS*,12*S*)-8-Acetyl-12-hydroxy-6-oxo-10-heptadecenoate (**24**): The silyl ester (**23**; 8 mg, 0.017 mmol) was similarly desilylated by treatment in a solution of $CH_3COOH$ (0.5 ml), $H_2O$ (0.2 ml), and THF (0.2 ml) at ambient temperature for 6 h to give **24** (2.5 mg, 0.007 mmol, 41%) after preparative TLC purification (cyclohexane: ethyl acetate=2: 3). *Rf* 0.25 (cyclohexane: ethyl acetate=1: 1). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3450, 1740, 1715, 965. NMR ($CDCl_3$) $\delta$: 0.89 (3H, bt, $J$=5 Hz, $C_{17}H_3$), 1.2—1.8 (12H, m), 2.23 (3H, s, $COCH_3$), 2.0—2.64 (9H, m), 3.0 (1H, bs, OH), 3.66 (3H, s, $COOCH_3$), 4.00 (1H, m, $C_{12}H$), 5.44—5.61 (2H, m, olefinic H). MS *m/e*: 354 ($M^+$), 336 ($M-H_2O$), 318, 305. High-resolution MS for $C_{20}H_{34}O_5$ ($M^+$): Calcd *m/e*: 354.2408; Found: 354.2320 and $C_{20}H_{32}O_4$ (dehydration peak from molecular ion): Calcd *m/e*: 336.2302; Found: 336.2283.

**(5*Z*,10*E*)-(8RS,12*S*)-12-Hydroxy-8-((*EZ*)-1-methoxyiminoethyl)-5,10-heptadecadienoic Acid (26)**——(a) Methyl (5*Z*,10*E*)-(8*RS*,12*S*)-12-Hydroxy-8-((*EZ*)-1-methoxyiminoethyl)-5,10-heptadecadienoate (**25**): A mixture of **7a**(*S*) (5 mg, 0.015 mmol) and methoxylamine hydrochloride (6 mg, 0.072 mmol) in pyridine (0.1 ml) was heated at 60°C for 3 h. After removal of the pyridine, the residual oil was subjected to preparative TLC ($CH_2Cl_2$: AcOEt=7: 3) to afford **25** (4 mg, 0.011 mmol, 73%). *Rf* 0.55 ($CH_2Cl_2$: AcOEt=7: 3). NMR ($CDCl_3$) $\delta$: 0.86 (3H, bt, $J$=6 Hz, $C_{17}H_3$), 1.1—1.8 (11H, m), 1.68 and 1.70 (3H, 2s, isomeric $CH_3C$=NO–), 1.8—2.5 (9H, m), 3.64 (3H, s, $COOCH_3$), 3.80 (3H, s, $=NOCH_3$), 4.04 (1H, m, $C_{12}H$), 5.34 (2H, m, olefinic H), 5.50 (2H, m, olefinic H). MS (trimethylsilylated **25**) *m/e*: 439 ($M^+$), 408, 368.

(b) (5*Z*,10*E*)-(8*RS*,12*S*)-12-Hydroxy-8-((*EZ*)-1-methoxyiminoethyl)-5,10-heptadecadienoic Acid (**26**): The above ester (**25**; 4 mg, 0.011 mmol) was similarly hydrolyzed with aqueous alcoholic NaOH to give **26**, which showed a single spot on TLC (*Rf* 0.70, $CH_2Cl_2$: acetone=7: 3).

## References and Notes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